PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	ISHII *et al.*	EXAMINER:	POPA, ILEANA
APPLICATION NO.:	10/680,356	ART UNIT:	1633
FILED:	OCTOBER 6, 2003	CONF. NO:	5651
FOR:	**SPATIALLY ENCODED AND MOBILE ARRAYS OF TETHERED LIPIDS**		

Pre-Appeal Brief Request for Review

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Sir:

This Pre-Appeal Brief Request for Review responds to the Office Action dated July 7, 2009 (hereafter "Final Office action") in the above-identified application. Because the rejection is based on both factual and legal error, Applicants request review of the outstanding rejections prior to filing an Appeal Brief. Applicants petition for a three-month extension of time in which to file this communication, to extend the date for response to and including January 7, 2010. A separate Petition is enclosed.

The Panel is directed to Applicant's response filed March 30, 2009 for a listing of the clams as pending and for a summary of the teachings of the cited prior art documents.

Rejections under 35 U.S.C. §103

Claims 1-4, 6, 7, 9, 11, and 12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* (PCT Publication No. WO98/23948) in view of both Boukobza *et al.* (*J Phys Chem*, 105:12165-12170, 2001) and Niemeyer *et al.* (DE 19902391, abstract).

Claims 1-4, 6, 7, and 9-12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* taken with both Boukobza *et al.* and Niemeyer *et al.*, in further view of each of Cornell *et al.* (U.S. Patent No. 5,874,316), Arnold *et al.* (U.S. Patent No. 5,310,648), and Bayerl *et al.* (U.S. Patent No. 6,051,372).

Claims 1-4, 6-9, 11, and 12 were rejected under 35 U.S.C. §103 as allegedly obvious over Boxer *et al.* taken with both Boukobza *et al.* and Niemeyer *et al.*, in further view of Shen *et al.* (U.S. Publication No. 2003/0148335).

These rejections are respectfully traversed.

A. Clarifying Certain Features of Pending Claim 1

Claim 1 as pending includes, inter alia, the features that:

i) the array of separated lipid bilayers comprises at least one biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotides, and

ii) the oligonucleotide tethered to each bilayer expanse has a sequence specific to that expanse.

B1. Addressing the Examiner's Basis for Maintaining the Rejection

The Examiner has maintained the rejection of the claims on the grounds that the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* provide a prima facie case of obviousness. As Applicants will show in point i) below, this is incorrect, and therefore the underlying rationale for maintaining the rejections is technically and legally flawed, as discussed in points ii) and iii) below.

i) The Examiner alleges on page 4 of the Final Office action that:

> Boxer et al. teach that biomolecules can be attached to the bilayer expanses via specific molecular interactions between complementary oligonucleotides, wherein each expanse comprises a specific oligonucleotide (claims 1 and 4) (p. 4 bridging p. 5, lines 1-5, p. 16, lines 3-21).

This reading of Boxer *et al.* is incorrect. The paragraph in Boxer *et al.* bridging page 4 and page 5, lines 1-5 states:

> The lipid bilayer expanses on different bilayer-compatible surface regions may have different compositions, and may further include a selected biomolecule, with different expanses having a different biomolecule, such as transmembrane receptor or ion channel. The biomolecule may be covalently or non-covalently attached to a lipid molecule. Examples of non-covalent interactions include electrostatic and specific molecular interactions, such as biotin/streptavidin interactions. Examples of biomolecules include proteins, such as ligands and receptors, as well as polynucleotides and other organic compounds.

In this passage, Boxer *et al.* describe that the *biomolecule* may be a polynucleotide, not that a biomolecule can be attached to the lipid array via complementary oligonucleotides, as the Examiner asserts. There is no mention in this passage, or any other passage in Boxer *et*

al., of using complementary oligonucleotides (or any nucleotide) to anchor a biomolecule to a lipid array.

Also in this passage, Boxer *et al.* state that the biomolecule may be covalently or non-covalently attached to a lipid molecule, and gives examples of attachment as electrostatic and specific molecular interactions, such as biotin/streptavidin interactions. No mention is made of complementary oligonucleotides as a means of attachment.

With respect to the other passage in Boxer *et al.* noted by the Examiner, p. 16, lines 3-21, the sentence on p. 16 lines 3-5 is the only reference in the passage to nucleic acids:

> As discussed above, the supported bilayers may contain receptors of other biomolecules, such as peptides, nucleic acids, factors, etc., attached to or incorporated into the supported bilayer membranes.

Again, this sentence refers to a nucleic acid biomolecule attached to the bilayer. It does not teach that a biomolecule is anchored to a bilayer via complementary oligonucleotides.

Thus, the Examiner's assertion that "Boxer et al. teach that biomolecules can be attached to the bilayer expanses via specific molecular interactions between complementary oligonucleotides" is incorrect.

ii) On page 5, lines 6-17, the Examiner alleges:

> It would have been obvious to one of skill in the art….to use the oligonucleotide hybridization as taught by Boxer et al. to tether vesicles to the array of separated lipid bilayers, with a reasonable expectation of success……because the prior art teaches that oligonucleotides are versatile and their use allows for the parallel immobilization of different macromolecules coupled to different nucleic acids (see Niemeyer, Abstract).

As set forth in point i) above, it is an incorrect assertion that Boxer *et al.* teach oligonucleotide hybridization to tether a biomolecule to a lipid array. Therefore, the basis for the Examiner's allegation that the cited art provides a prima facie case of obviousness is grounded in a technically incorrect understanding of Boxer *et al.*. Accordingly, it is legally in error to assert that the combined teachings of the cited art provides a prima facie case of obviousness.

iii) In the Final Office action, on page 6, the Examiner alleges that Applicants have failed to address the combination of cited references, by instead arguing the references individually. To ensure the record is clear that Applicants have addressed the fact that the

combination of cited references fail to establish a prima facie case of obviousness, the following points are reiterated.

Legal Standard for Prima Facie Obviousness

To support an obviousness rejection, MPEP §2143.03 requires "all words of a claim to be considered" and MPEP § 2141.02 requires consideration of the "[claimed] invention and prior art as a whole." Further, the Board of Patent Appeal and Interferences recently confirmed that a proper, post-KSR obviousness determination still requires the Office make "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *Ex parte Wada and Murphy*, Appeal 2007-3733 (2008), citing *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) and *CFMT v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003). "It is well settled that the 'Patent and Trademark Office (PTO) must consider all claim limitations when determining patentability of an invention over the prior art.'" *Ex parte Wada and Murphy*, Appeal 2007-3733 (2008), citing *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

The Combined Teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* Fail to Satisfy the Legal Standard for a Prima Facie Case of Obviousness

As noted above, pending claim 1 includes the features that:

a) the array of separated lipid bilayers comprises *at least one biomolecule anchored* to a lipid bilayer expanse *through complementary oligonucleotides*, and

b) the oligonucleotide tethered to each bilayer expanse has a sequence specific to that expanse.

The combined teachings of the cited references fail to show or suggest at least these two features of claim 1.

As discussed in detail in point i) above, Boxer *et al*. fail to show or suggest a biomolecule anchored to a lipid bilayer through complementary oligonucleotides.

Therefore, to establish a prima facie case of obviousness, this claim feature must be provided by one of the other cited references, Boukobza *et al*. or Niemeyer *et al*. To determine whether either of these cited secondary and tertiary references provide the feature of a biomolecule anchored to a lipid bilayer through complementary oligonucleotides, it is necessary to read each reference individually and consider its teaching. Without intending

to argue each reference separately, Applicants briefly state here what each reference describes and therefore why it fails to provide the requisite feature.

Boukobza *et al*. teach using *biotin-avidin affinity* for binding liposomes to surface supported bilayers. Boukobza *et al*. do not show or suggest anchoring by means of complementary oligonucleotides. Therefore, this reference combined with Boxer *et al*. does not show or suggest the features of claim 1.

The abstract of Niemeyer *et al*. fails to teach or suggest anchoring a biomolecule through complementary oligonucleotide sequences. The Niemeyer *et al*. abstract mentions the use of "nucleic acids as immobilization-mediating reagents", but not of using complementary oligonucleotide sequences. Reference to "nucleic acids as immobilization-mediating reagents" is not equivalent to complementary hybridization of nucleotides, but simply a reference to a biomolecule attached to a nucleic acid that is immobilized on a solid support. Nothing in the abstract expressly or inherently states complementary binding of nucleotides. Therefore, this reference combined with Boxer *et al*. and/or with Boukobza *et al*. does not show or suggest the features of claim 1.

Accordingly, and with respect to the rejection of claims 1-4, 6, 7, 9, 11, and 12 based on the combination of Boxer *et al.*, Boukobza *et al.*, and Niemeyer *et al.*, the combined teachings of these documents fail to show or suggest at least one biomolecule anchored to a lipid bilayer expanse through complementary oligonucleotide sequences as presently claimed.

Rejections Based on the Addition of Cornell *et al.*, Arnold *et al.*, Bayerl *et al.* or Shen *et al.* also do not establish a prima facie case of obviousness

The Examiner cites Cornell *et al.*, Arnold *et al.*, Bayerl *et al.* and Shen *et al.* for the sole purpose of providing features of dependent claims 8 and 10. Thus, for the prima facie case of obviousness to stand, the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* must provide all of the features of claim 1. For the reasons given above, it is abundantly clear that the combined teachings of Boxer *et al.*, Boukobza *et al.* and Niemeyer *et al.* do not provide all of the features of claim 1. Therefore, a prima facie case of obviousness of claims 8 and 10 has not been established.

Accordingly, the combination of cited documents fail to teach each and every claimed feature as claimed. Applicants submit that the obviousness rejections are in error and should be withdrawn.

Respectfully submitted,
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